REMARKS

Entry of the foregoing, reexamination and reconsideration of the above-identified application are respectfully requested.

The claims have been amended to correct a minor inadvertent error. The claims were previously amended to identify SAM 2197 as belonging to *Mortierella alpina*. This identification, however, was in error. As identified in the specification as well as the deposit information provided in the application, SAM 2197 as belonging to *Mortierella sp.* The claims have been amended accordingly to correct this inadvertent error.

New claims 35-37 have also been added. In claim 35, the microorganism is identified as being "of the genus *Mortierella,* subgenus *Mortierella"* in accordance with the teachings of the specification. In claim 36, the microorganism is identified as being "selected from section *Alpina,* section *Hygrophila,* section *Mortierella,* section *Schmuckeri,* section *Simplex,* section *Spinosa* and section *Stylospora*"

Further, it is noted that the Declaration dated August 7, 2003, also inadvertently referred to SAM 2197 as *Mortierella alpina.* A corrected Declaration correctly identifying SAM 2197 as *Mortierella sp.* is being filed herewith.

The Official Action noted that non-elected claims 8, 10-15 and 17-30 were still pending in the application and requested that they be deleted at this time. As indicated in the Claim Summary, these claims are being deleted herein.

Applicants note with appreciation the indication that claim 34 is deemed to be allowable. The Official Action states that, since data has been shown for this species, the

use of this species in a method as claimed would not have been obvious. For the reasons set forth herein, claims 1, 3-7 and 33 should also be in condition for allowance.

Claims 1, 6, 7 and 33-34 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kyle. This rejection is respectfully traversed.

The Official Action states that the previously submitted "Experimental Report" is not probative since it is not in Declaration form. Enclosed herewith is the information from the "Experimental Report" in Declaration form, i.e., a Declaration Under 37 C.F.R. §1.132 by Dr. Akimoto. The Declaration should be found probative of the non-obviousness of Applicants' invention. For at least the reasons set forth herein, Kyle et al fails to disclose or even suggest the instantly claimed invention.

The Akimoto Declaration clearly shows that Kyle et al is not a process within the scope of the claims since the microorganism disclosed in Kyle will not produce arachidonic acid in the amount required to fall within the scope of the claims. Nor is there any suggestion in Kyle et al to use a microorganism resistant to high carbon concentrations, or that such high amounts of arachidonic acid could be obtained. As such, Kyle cannot disclose or even suggest the instantly claimed invention.

Moreover, contrary to the assertion in the Official Action, the Kyle strain of *Mortierella alpina* is not "resistant" to a high concentration of carbon. If the Kyle et al strain was resistant, a higher amount of arachidonic acid would have been achieved when cultured according to the conditions of the declaration, as did the two resistant strains exemplified therein. As set forth above, the Declaration clearly shows that Kyle et al does

not teach a microorganism that could be used in the instantly claimed invention. The strain identified in Kyle produces only 4.0 g/L arachidonic acid, as shown in Table 1 of the Declaration.

It is further noted that the Kyle et al reference does not teach the particular conditions of "a medium having a carbon source concentration of at least 4% by weight at the start of culturing and the addition of at least an additional 6% by weight of carbon source during the culturing." Since these particular conditions are not described in the reference, the claimed process is not disclosed. Nor is there any suggestion to employ the starting carbon concentration and then add an additional at least 6% by weight carbon.

Regarding the Experimental Report, the Official Action states that it shows that the two exemplified strains grown in media containing 4% glucose produce a better yield of arachidonic acid. The Official Action asserts, however, that "there is no clear nexus between culturing any *M. alpina* having resistance to a carbon source of high concentration, in a certain medium, and the production of 7 g/l of arachidonic acid." The Declaration submitted herewith should overcome these assertions in the Official Action.

The nexus between culturing a microorganism having resistance to a carbon source of high concentration and the production of at least 7 g/l of arachidonic acid is described in the Declaration at Paragraphs 8-11. As explained by Dr. Akimoto:

8. Theoretically, the maximum amount of cultured cells should increase as the total concentration of a carbon source in a culture medium increases. As a

result, the total amount of product, i.e., arachidonic acid, should increase as the total concentration in culture medium.

9. However, in practice, a high concentration of carbon source inhibits the growth of the producer microorganism. As a result, the maximum level of product is limited. In the case where a microorganism having lower resistance to carbon source concentration is used, the growth of cells stops at a lower level of cell concentration, even if a culture medium contains a high level of carbon source concentration, due to inhibition by the carbon source. As a result, the maximum level of the product is low.

10. On the other hand, in the case where a microorganism having higher resistance to carbon source concentration is used, the growth of cells stops at a higher level of cell concentration, if a medium contains a high level of carbon source concentration. As a result, the maximum level of the product is high.

Thus, by using a microorganism having high resistance to carbon, arachidonic acid can be produced in high amounts as claimed.

The Akimoto Declaration shows the success of two strains of genus *Mortierella,* subgenus *Mortierella,* when cultured according to the claimed method. That two microorganism were tested and found to produce arachidonic acid in accordance with the claimed methods, should show that there is a nexus between microorganism resistance to a carbon source of high concentration and production of a high amount of arachidonic acid,

i.e., at least 7 g/L. This showing together with the explanation by Dr. Akimoto should be sufficient to establish a nexus and support the full scope recited in the instant claims.

The theory behind the instant invention is further explained in the instant specification. As stated in the specification, "at 4% by weight of carbon source concentration, conventional microorganisms belonging to the genus *Mortierella*, subgenus *Mortierella* (such as *Mortierella alpina* IFO 8568) and having been conventionally used for the production of arachidonic acid, dihomo-γ-linolenic acid and/or eicosapentaenoic acid lower their growth level, and at 8% by weight of carbon source concentration, the above-mentioned conventional microorganisms cannot grow."

This is shown in the Akimoto Declaration. As shown in Table 1, when the *M. alpina* microorganism identified in Kyle et al, *i.e.*, ATCC 42430 (*See,* Example 2), was cultured according to the instantly claimed invention, only 4.0 g/L arachidonic acid was produced. This result can be compared with the amount of arachidonic acid produced in accordance with the instant invention by a *Mortierella* microorganism resistant to high carbon concentration. By contrast with the microorganism of Kyle et al, when two microorganisms in accordance with the instant invention were cultured, over 7 g/L of arachidonic acid was obtained.

The specification discloses similar results. For example, on page 3, lines 3-15, it is disclosed that a *Mortierella* microorganism produced 4.09 g/L arachidonic acid at a glucose concentration of 2% after 7 days, and 2.3 g/l when cultured at a glucose concentration of 4.3% for 3 days. Page 3, lines 16-31, of the specification discloses that only 1.5 g/L of

arachidonic acid was produced with a dextrose concentration of 9.8% after 7 days, and 9.1 g/L after culturing for 16 days at 9.8% dextrose. The specification further sates that "[t]he growth of the microorganism was particularly poor due to a high initial dextrose concentration, and the production amount of arachidonic acid after culturing for 7 days was as low as only 1.5 g/L." Page 3, lines 26-30.

The specification further discloses that in WO 96/21037, only 5.3 g/L of arachidonic acid was produced after culturing for 8 days with an initial glucose concentration of 10%. However, to achieve even this amount of arachidonic acid, additional procedures such as pH control and addition of salts were used and complicated operations were required. *See,* page 4, line 32 - page 5, line 2.

The instant invention was made to overcome such problems of low production and complicated procedures:

> Accordingly, it has been desired to develop a method for producing arachidonic acid, dihomo-γ-linolenic acid or eicosapentaenoic acid efficiently with simple operations and in a large amount by finding a microorganism which is resistant to a carbon source of high concentration at the starting stage and which shows a sufficient growth level even in a medium having a high initial glucose concentration, and using the microorganism.

Page 4, lines 28-36.

Moreover, one skilled in the art could readily test microorganisms to determine whether they have resistance to high carbon concentration.

That *Mortierella* microorganisms having resistance to a carbon source of high concentration could be used in a method as claimed is not taught or suggested by Kyle et al. Nor does Kyle et al disclose or suggest that at least 7 g/L of arachidonic acid could be

obtained by culturing the microorganism under conditions with a carbon source of at least 4% by weight at the start and further adding an additional 6% by weight of carbon source during the culturing. There is no suggestion in Kyle et al to use at least 4% by weight of carbon source and to then add an additional 6% by weight of carbon source.

Furthermore, the showing of two species of the instant invention is sufficient to show the difference between the claimed invention and Kyle et al, as well as the unexpected results of the instant invention. It would be recognized by one skilled in the art that other *Mortierella* microorganisms having a resistance to a carbon source of high concentration, when cultured according to the claimed invention, could also produce arachidonic acid at a level of at least about 7 g/L. One skilled in the art could readily test the microorganisms and determine whether the product is being produced in accordance with the method as claimed. Only such microorganisms of the species *Mortierella* that, when cultured according to the claimed invention, produce arachidonic acid at a level of at least about 7 g/L fall within the scope of the claim.

By culturing the microorganism in high carbon concentrations it can readily be determined whether it is resistant to carbon. It is also readily determined whether the claimed process is being met by measuring the arachidonic acid produced. In view of the showing of two microorganisms that meet the claimed limitations, and a specified manner for one skilled in the art to determine whether or not the claimed limitations are met, *i.e.*, upon measuring the amount of arachidonic acid produced, it is readily determined whether

the process falls within the scope of the claimed invention. Thus, it is believed that the showing of the Declaration is commensurate with the scope of the claims.

Kyle et al further teaches away from the present invention. In Kyle et al, pH controls are used during its process for producing arachidonic acid. Such pH controls are not needed in the instant invention. The specification specifically states that the microorganism used in the instant invention "show[s] a high growth level without using complicated operations such as pH control and addition of inorganic salts." Page 5, lines 23-28. Since pH controls are used in Kyle et al, it further shows that the microorganism of the reference is not itself resistant to high carbon concentration, as required by the claims.

In view of the above, withdrawal of the rejection under §103(a) over Kyle et al is respectfully requested. Such action is believed to be in order.

It is respectfully submitted that all rejections have been overcome by the above amendments. Thus, a Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this amendment or the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at (650) 622-2360 so that prosecution of the application may be expedited.

Respectfully submitted,

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